08

Industry Study:

Insights into the Human Vaccine Market

Introduction:

A human vaccine is a type of biological substance that aims to prevent diseases by introducing weakened, killed, or fragmented microorganisms into the body. Its primary function is to activate the immune system, prompting the production of antibodies that can fight against specific pathogens and offer protection against future infections. Human vaccines can be found in various forms, such as liquid solutions, powdered form stored in vials, pre-filled syringes, or capsules.

Vaccine Types:

Human vaccines are classified based on the specific biological components they utilize to induce immune protection against pathogens within the human body. There are six distinct types of vaccines, each employing different biological mechanisms. These categories include:

There are **6** types
of human vaccines with different biological platforms

1. Live Attenuated Vaccines

Certain vaccines replicate the effect of a natural infection by utilizing a weakened version of a live virus or bacteria. These are known as live attenuated vaccines and are capable of inducing robust and long-lasting immunity. Unlike some other vaccines, live attenuated vaccines usually do not necessitate multiple doses or booster shots. For instance, the measles, mumps, and rubella (MMR) vaccine exemplifies this type of vaccine.

2. Inactivated Vaccines

Such vaccines consist of pathogens that have been rendered inactive. Usually, multiple doses of these vaccines are needed to establish and maintain immunity. The rabies vaccine serves as an example of this type of vaccine.

3. Subunit, Recombinant, or Protein Vaccines

These vaccines utilize components of a pathogen, such as proteins, sugars, or the germ's outer casing (capsid), to stimulate the immune system and generate immunity. Similar to inactivated vaccines, multiple doses may be required to establish ongoing protection. However, these vaccines are suitable for a broad range of individuals, including those with compromised immune systems and chronic health conditions. An example of this type of vaccine is the human papillomavirus (HPV) vaccine.

4. Toxoid Vaccines

To generate immunity, these vaccines employ an inactivated form of a toxin, known as a toxoid, which mimics the toxins produced by certain bacteria. A prime example of this type of vaccine is the tetanus and diphtheria vaccine.

5. Messenger Ribonucleic Acid (mRNA) Vaccines

mRNA vaccines utilize the genetic material (mRNA) of the pathogen to prompt human cells to produce a specific protein, which then triggers an immune response. An example of this type of vaccine is the COVID-19 vaccine.

6. Viral Vector Vaccines

Viral vector vaccines employ harmless viruses to transport genetic material from the targeted pathogen into the body, stimulating an immune response and promoting immunity. The Ebola vaccine serves as an illustration of this type of vaccine.

All human vaccine types require multiple doses throughout time to maintain continuous immunity against illnesses

Each category of human vaccines has its own advantages and disadvantages, which can influence the decision of manufacturers regarding their production. With the exception of live attenuated vaccines, all vaccine types require multiple doses or booster shots over time to maintain continuous immunity against diseases. Vaccines containing live germs may not be suitable for individuals with weakened immune systems or certain long-term health conditions. Specific vaccines, like mRNA and live virus vaccines, require constant refrigeration during storage and transportation. Notably, the production process can vary in complexity depending on the vaccine type. Nucleic acid vaccines, such as mRNA vaccines, can be developed and manufactured more quickly compared to other types of vaccines.

Overall, vaccine development is a rigorous and time-consuming process in which safety and efficacy are prioritized at every stage. To bring safe and effective vaccinations to the public, it often takes years of research and collaboration among scientists, regulatory authorities, and manufacturers.

Human Vaccine Supply Chain:

The vaccine supply chain is a highly organized system that enables smooth and efficient distribution of vaccines to the public, starting from the manufacturing facilities. The entire supply chain typically involves three or four stages, depending on the specific vaccine. These stages include drug discovery, mass production, distribution, and reverse logistics. The diagram below illustrates the different stages of the vaccine supply chain.

Drug discovery and development process	Mass production	Distribution and administration	Reverse logistics
» Drug Discovery » Pre-clinical trials » Clinical trials » Approval by regulators	» Selection of suppliers » Ingredient and reagent sourcing » Quality checking » Drug manufacturing » Primary packaging (vials, rubber stoppers)	» Secondary packaging (cold chain equipment) » Warehousing (own or outsourced) » Transportation » Storage (freezers) » Adminstration (syringes, vials)	» Returned cold chain equipment

*Note, for illustrative purposes only as the supply chain will differ across different vaccines.

**Source: Organization for Economic Co-operation & Development (OECD) - Manufacturing and distributing vaccines publication.

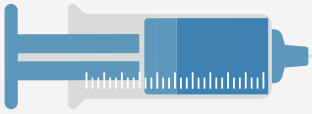
The drug discovery and mass production stages require qualified professionals and sophisticated facilities

Certain vaccines, such as those containing live viruses, may require temperature-controlled storage during transportation. In such cases, a cooling box is used to ensure the integrity of the vaccine. Once the vaccine reaches its intended destination, the cooling box is returned to its original location, marking the reverse logistics stage of the supply chain. This stage involves the retrieval and management of the cooling boxes to maintain the efficiency of the vaccine distribution process.

The various stages of the supply chain for vaccines are often geographically dispersed. While the drug discovery and mass production stages necessitate specialized expertise and advanced facilities, leading to their concentration in specific locations, the distribution stage entails the sourcing of secondary packaging materials, warehousing, storage, and administration items from multiple global sources. The following diagram illustrates the complete journey of a vaccine, encompassing all stages of the supply chain.

The Human Vaccine's Journey

Steps and Stages of Vaccine Preparation



01 Bacteria or virus
The antigens are developed using raw material

02 Harvesting
The antigens produced from microorgansims are extracted

03 Purification
Impurities are removed and concentrated through physical and chemical processes

04 Inactivation
Pathogenicity is suppressed while retaining immunological properties

05 Valence assembly
The active antigenic substances are combined in a single component

06 Formulation
All the ingredients are melt together

07 Filling
The vaccine is filled into a vial or a syringe

08 Freeze-drying
Removing the water in a product by transforming it into powder, which ensures a better stabillity and conservation

09 Packaging
The vaccine is labeled in accordance with regulatory requirements and packed, ready for shipping

10 Batch release
Quality assurance confirms the product is manufactured and tested in accordance with the correct procedures. The national regulatory authority gives authorization to release product for distribution

11 Transport
Our vaccines are distributed all around the world, respecting the cold chain and temperature between 2°C and 8°C

Source: Sanofi "The vaccine's journey" Infographic. https://sanofi.com

International Market Highlights:

529 SAR billion

The WHO estimated the global human vaccine market in 2021

In 2021, the global human vaccine market was estimated by the World Health Organization (WHO) to be valued at SAR 529 billion, with around 16 billion vaccine doses provided. This accounted for 10% of the overall pharmaceutical market, which had a value of SAR 5.29 trillion. If we exclude the COVID-19 vaccine doses, the global vaccine market value decreases to SAR 158 billion, with approximately 5.3 billion doses administered. As a result, the vaccine market represents 4% of the total pharmaceutical market.

Comparing the figures to 2019, the vaccine market showed growth in value. In 2019, it was valued at SAR 143 billion, with 5.8 billion doses administered, and accounted for 4% of the total pharmaceutical market. The differences between 2019 and 2021 can be primarily attributed to a decline in the administration of pediatric vaccines and an increase in the usage of higher-priced adult vaccines.

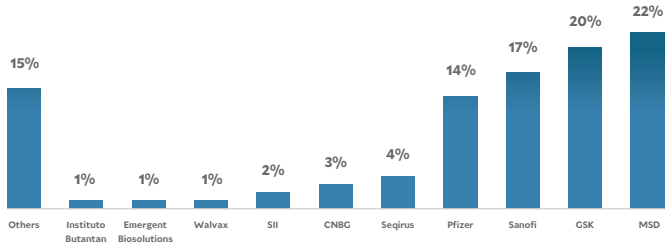
Global Human Vaccine Market - Major Players

30%

Pfizer market share in 2021

According to the WHO, Pfizer had the largest market share (30%) in 2021, followed by Moderna (12%) and Sinovac (12%). Excluding COVID-19 vaccines alters the vaccine supply landscape, with Merck Sharp & Dome (MSD) gaining the largest market share (22%) followed by GSK (20%) and Sanofi (17%). The top 10 manufacturers by value, including and excluding COVID-19, are shown in the figures below:

Top 10 Manufacturers by value (excluding COVID-19), 2021



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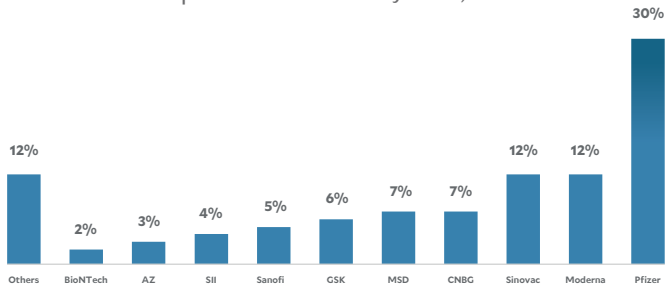


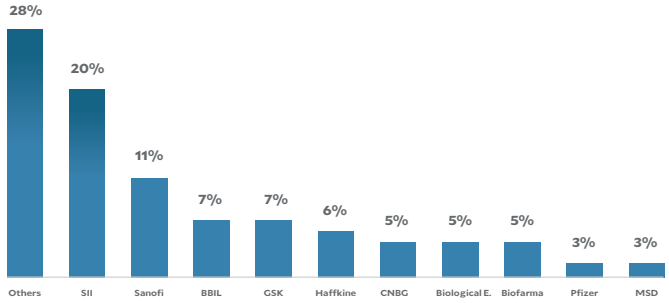
sourced: WHO Vaccine Market Report 2022

16%

Pfizer was also the leading manufacturer by volume in 2021

Pfizer was also the leading manufacturer by volume (16%) in 2021, followed by Serum Institute of India (SII) (15%) and Sinovac (13%). Excluding the volume of the COVID-19 vaccine, places SII as the top manufacturer by volume (20%) followed by Sanofi (11%), Bharat Biotech (BBIL) (7%) and GSK (7%). The top 10 manufacturers by volume, including and excluding COVID-19, are shown in the figures below:

Top 10 Manufacturers by volume (excluding COVID-19), 2021



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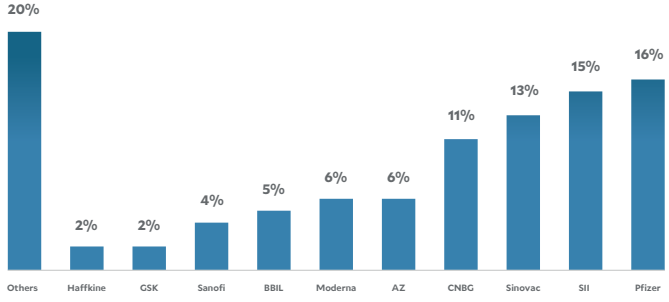

sourced: WHO Vaccine Market Report 2022

Excluding COVID-19 vaccines, the top manufacturers in terms of both value and volume are Serum Institute of India (SII), China National Biotechnology Group (CNBG), Sanofi, GSK, Merck Sharp & Dome (MSD), and Pfizer. These manufacturers have consistently maintained their positions in the top 10 since 2019 and continue to dominate the global market in terms of market value and volume. Despite the emergence of new players in the global vaccine market during the COVID-19 pandemic, the industry remains highly concentrated and reliant on a small number of manufacturers.

94 manufacturers

were distributing vaccines to WHO Member States

Out of the 94 manufacturers distributing human vaccines to WHO Member States, the majority were located in the WHO Western Pacific region (41%), followed by the WHO European region (21%), and the WHO Americas region (17%). However, the Eastern Mediterranean region, which includes 22 countries including Saudi Arabia, had a significantly lower number of manufacturers, accounting for only 7% of the total 94 manufacturers.

KSA Market Highlights:

Saudi Arabia's human vaccine landscape is completely dominated by multinational vaccine manufacturers, with only a single local production facility

The human vaccine industry in Saudi Arabia is predominantly controlled by multinational vaccine manufacturers, with only one local production facility. In 2021, Sanofi, GlaxoSmithKline (GSK), and Pfizer held a combined market share of over 90% in the country, with Sanofi and GSK alone accounting for 70% of the market. This aligns with the global vaccine market, where the top five vaccine producers hold 77% of the market share.

In the Saudi Arabian vaccine market in 2021, the combined market value of the top five most requested vaccines accounted for 83% of the total, and these vaccines are the pneumococcal conjugate vaccine (PCV), meningococcal conjugate vaccine (MCV), rotavirus vaccine (RV), varicella zoster vaccine (VZV), and the diphtheria, tetanus, pertussis, polio, haemophilus influenzae type b, and hepatitis b (DTaP/IPV/Hib/HepB) vaccine.

The vaccines listed above are included in the national immunization schedule of the Ministry of Health (MOH). These vaccines are sourced from global pharmaceutical companies such as GlaxoSmithKline (GSK), Sanofi, and Pfizer as they are imported into Saudi Arabia.

GlaxoSmithKline (GSK)

In 2021, GSK supplied over 76% and 97% of total dose demand (by value) for RV and VZV, respectively

In 2021, a significant majority of the requested doses for RV and VZV vaccines, accounting for 76% and 97% respectively in terms of value, were supplied by GSK. Similarly, Sanofi provided 99% of the requested doses for MCV vaccine and 95% for DTaP/IPV/Hib/HepB vaccine. Additionally, Pfizer supplied over 99% of the requested doses for PCV vaccine. These statistics demonstrate that Saudi Arabia heavily depends on international pharmaceutical companies to meet its vaccination demands for the national immunization program.

3%

Saudi vaccine market is estimated to grow by a CAGR of 3% in the next five years

As the occurrence of new and previously known infectious diseases increases worldwide, there is a growing anticipation for higher demand for human vaccines. This can be attributed to factors such as increased travel and higher population density in many areas, which contribute to the spread of these diseases. Additionally, there is an expected rise in the demand for region-specific vaccines, including halal variations. Gelatin, which is derived from the boiling of animal skin and bones, including cows, is commonly used in certain vaccines as a stabilizing agent. However, in halal vaccines, gelatin sourced from bovine animals is used as a substitute for non-halal ingredients.

Due to the expanding population in the Kingdom of Saudi Arabia, there is an expected increase in the demand for vaccines in the local market. The population in Saudi Arabia has grown by approximately 1.2% between mid-2020 and mid-2021, according to the General Authority for Statistics (GAS). This demographic shift may result in a greater requirement for pediatric vaccinations to cater to the needs of the growing population. It is estimated that the vaccine market in Saudi Arabia will witness a compound annual growth rate (CAGR) of 3% over the next five years.

Human Vaccine	2023	2024	2025	2026	2027
Demand (SR thousands)	1,858,738	1,914,500	1,971,935	2,031,093	2,092,026

الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

In the Kingdom, the Saudi Food and Drug Authority regulates human vaccine selling prices

Multinational companies that produce human vaccines often adopt a tiered pricing approach, where the pricing of vaccines is determined based on the income level and financial capacity of different countries. This means that the same vaccine may be sold at a higher price to wealthier countries and at a lower price to developing countries. In the Kingdom of Saudi Arabia, the selling prices of human vaccines are regulated by the Saudi Food and Drug Authority (SFDA).

The National Unified Procurement Company is responsible for sourcing and purchasing medication and medical devices in the Kingdom

Vaccines are priced on a per-dose basis and the price may vary depending on factors such as the type of vaccine, the income group of the purchasing country, the procurement method, and the terms of the contract. In the Kingdom of Saudi Arabia, the National Unified Procurement Company (NUPCO) is responsible for sourcing and purchasing medications and medical devices. Regarding the top five most sought-after vaccines in the country, the cost per dose is provided in the table below. It is important to note that most vaccines require multiple doses to achieve immunity in an individual.

Vaccine Type	Vaccine name	Type	Price	Manufacturer
MCV	MENACTRA	Vial	246	SANOFI PASTEUR
VZV	VARILRIX	Vial	167	GLAXOSMITHKLINE
RV	ROTARIX	Pre-filled syringe	182	GLAXOSMITHKLINE
DTaP/IPV/Hib/HepB vaccine	HEXAXIM	Vial	173	SANOFI PASTEUR
PCV	PREVENAR 13	Pre-filled syringe	246	PFIZER

Source: SFDA Drug List

To be eligible to operate in Saudi Arabia, all local factories must first meet the "Good Manufacturing Practice" criteria

The Saudi Food & Drug Authority (SFDA) is in charge of overseeing and supervising the human vaccine industry in Saudi Arabia. SFDA has implemented numerous laws and regulations to regulate this sector. Local factories are required to meet the "Good Manufacturing Practice" standards in order to be permitted to operate in Saudi Arabia. Additionally, human vaccines must obtain Market Authorization Approval from SFDA before they can be sold and distributed in the Saudi market.

Saudi Arabia is actively working towards establishing local production of human vaccines. On July 6th, 2023, the Arab Company for Pharmaceutical Products (Arabio), Sanofi, and Lifera (a biopharmaceutical company owned by the Public Investment Fund (PIF)) entered into a Memorandum of Understanding (MOU) with the aim of developing local vaccine manufacturing capacity. According to the MOU, Lifera will serve as a contract manufacturer for Sanofi and Arabio, while Tamer Group (a significant shareholder of Arabio) will handle local and regional vaccine distribution needs.

In May 2023, SaudiVax, a biopharmaceutical company based in Saudi Arabia, entered into a partnership with the Human Resources Development Fund (HRDF) to develop a biomanufacturing training program. The objective of this program is to equip individuals with the necessary knowledge and skills to pursue careers in the biopharmaceutical industry. The training program commenced in June 2023 and has recently been accredited by the Saudi Commission for Health Specialties (SCFHS).

Challenges:

In light of the global impact of the COVID-19 pandemic, numerous nations, including Saudi Arabia, have acknowledged the significance of establishing domestic capacities for manufacturing human vaccines. As an integral part of its Vision 2030 strategy, the Kingdom aims to increase the localization of drug production from the existing 35% to 40%. The focus will be on prioritizing the production of routine vaccines for children and other highly sought-after medications.

As part of the Vision 2030 strategy, the Kingdom aims to localize 40% of drug production

The vaccine manufacturing industry poses significant challenges, as even the most rudimentary steps involved in producing vaccines that are safe, effective, and consistent throughout their lifespan can be immensely difficult to execute. The effectiveness of a vaccine can vary greatly due to a multitude of factors, including the inherent biological variations in the starting materials, the characteristics of the microorganism itself, the environmental conditions during microbial cultivation, the expertise of the manufacturing technician, and the intricacies of the purification processes. Furthermore, regulatory bodies not only approve specific vaccines but also examine and authorize the entire manufacturing, testing, and release procedures associated with those vaccines. Even a minor alteration in the production process can have profound implications on the final product, impacting its purity, safety, or effectiveness. The compounded complexity arising from biological and physical variability sets vaccine manufacturing apart from the production of conventional small molecule pharmaceuticals. Consequently, the number of successful and thriving vaccine manufacturers remains low despite the global demand for various vaccines remaining unmet.

Vaccine R&D and manufacturing requires a large initial investment and is considered a risky investment

Establishing a vaccine production facility presents several challenges on the commercial, technological, and regulatory fronts. Firstly, specialized equipment, clean rooms, and containment rooms are essential requirements for such facilities. However, there is a global shortage of personnel possessing the precise combination of skills, expertise, knowledge, competence, and suitable personalities to effectively operate vaccine production lines. While countries like Brazil, China, and India have made notable progress in this regard, many developing nations face limitations in their educational systems, resulting in a scarcity of qualified candidates. Consequently, vaccine manufacturers in these countries often rely on expatriate staff to ensure uninterrupted production. To successfully build a vaccine manufacturing plant, it becomes imperative to address these challenges through appropriate means.

- Vaccine R&D and manufacturing requires a large initial investment and is considered a risky investment as only a small fraction of developed vaccines receive regulatory approval.
- Vaccine development, research and registration can take several years and therefore realization of costs requires time.
- Vaccine pricing must strike a balance between accessibility and profitability. There must be a willingness from government and non-government organizations to subsidize vaccine costs to ensure successful commercialization.
- Stringent regulatory requirements, including World Health Organization (WHO) prequalification and local regulations combined with quality assurance (QA)/quality control(QC) requirements, are significant drivers of cost and require well-trained staff that can adapt to any regulatory changes.
- Certain vaccines require precise temperature control throughout the supply chain which introduces logistical challenges especially in remote or resource limited areas.
- Vaccine supply chain is vulnerable to disruption as various stages of the supply chain are carried out in different geographical regions.
- Public perception, misinformation and hesitancy can affect vaccine demand and acceptance.

Any new investor in the vaccine industry should have a broader vision for the future and encourage & support R&D

Two potential solutions have been proposed to address these challenges. The first option is to establish local vaccine production plants in collaboration with international vaccine companies through strategies such as in-licensing or joint venture partnerships. This approach would help overcome barriers related to expensive vaccine discovery, research, and development. An alternative approach involves initially setting up local plants as downstream manufacturing facilities, specifically for the filling and finishing stages of the vaccine production process. The aim of this approach is to foster collaboration between local plants and reputable pharmaceutical companies. It also encourages local facilities to gain expertise in running a factory that meets the requirements of both upstream and downstream supply chains for vaccines. To ensure the success of these strategies, new investors in the vaccine industry should adopt a broader vision for the future and actively support research and development efforts. The potential rewards of developing a new molecule or formulation in the vaccine field can be significant, but it requires patience, substantial investments, and comprehensive research to achieve the desired goals.